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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,291	01/17/2002	Heidi Stuhlmann	A31200-A - 070165.0467	7117

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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 08/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/053,291	STUHLMANN ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

8.80

DETAILED ACTION

Applicant's arguments filed 6-13-05 have been fully considered but they are not persuasive.

Claims 7-25 have been canceled. Claims 1-6 remain pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Oath/Declaration

A copy of the original oath/declaration filed in parent application 09/083290 was filed with the instant application.

Specification

The preliminary amendment filed 1-17-02, has been entered. Applicants amended the paragraph beginning on pg 14, line 16, by filling in the blanks with a date and ATCC Accession Nos. on page 15. Proof of deposit provided by applicants indicates Plasmids mVezf1.1, mVezf1.2 and mVezf1.N were designated ATCC Accession Nos: 209873, 209874 and 209875, respectively, on May 19, 1998.

Claim Rejections - 35 USC § 101

Claims 1-6 remain rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility for reasons of record.

The specification states the DB1 gene is expressed in human blood cells and adult organs, but the function of the DB1 protein is unknown (pg 6, ¶ 3, of the present specification). The specification states the Vezf1 gene is 98% homologous with the DB1 gene and is expressed during vasculogenesis and angiogenesis (pg 41 and 42). The specification does not provide a function for the Vezf1 or DB1 proteins. It is not clear that the homology between Vezf1 and DB1 is sufficient to give the protein products the same activity. The specification does not compare the homologies of Vezf1 or DB1 proteins with any protein with a known function such that the function of Vezf1 or DB1 could be determined with any certainty. While the DNA claimed in the instant invention may be used to make protein or to test for gene expression, such a use is not of value if the function of the protein is unknown. Without a readily apparent utility for the protein, it is unclear that the purified and isolated Vezf1 gene (claim 1), the purified and isolated nucleic acid encoding the Vezf1 protein (claim 3) or the expression vector containing the DB1 gene (claim 6) have any utility. The Vezf1 gene and the DB1 gene do not have a known function in the instant invention and consequently do not have a readily apparent utility.

Applicants argue by requiring that the specification and the art at the time of filing show Vezf1 expression occurs only in endothelial cells, the Examiner is improperly requiring perfect utility. Applicants' argument is not persuasive. The Examiner is not requiring that the specification and the art at the time of filing show aVezf1 expression occurs only in endothelial cells. The Examiner is merely pointing out that the asserted utility in the specification, using the Vezf1 gene or protein as a marker for endothelial

cells (pg 7, lines 11-13), was not a specific or substantial utility because Xiong taught Vezf1 was restricted to vascular endothelial cells and their precursors (1st line of abstract). "Endothelial cells" encompass any layer of epithelial cells that line the cavities of the heart, the lumena of blood and lymph vessels, and the serous cavities of the body (see Dorlands Medical Dictionary definition of "endothelium"). Serous cavities of the body include those enclosed by the pericardium, peritoneum, or pleura, not communicating with the outside of the body, and whose lining membrane secretes a serous fluid (see Dorlands Medical Dictionary definition of "serous cavity"). Thus, one of skill reading the specification would assume the genus of "endothelial cells" encompassed endothelial cells found in blood vessels, lymph vessels, salivary glands, the pericardial membrane, the peritoneal membrane, the pleural membrane and other serous glands. The Vezf1 gene, however, can only be used as a marker for vascular endothelial cells, which is considered essential to use the gene as a marker. Thus, the asserted utility in the specification is not a specific utility because the asserted utility is not specific to the one species within the genus. In other words, one of skill would not have been able to guess the species of "vascular endothelial cells" within the numerous species encompassed by "endothelial cells" or guess that the genus of "endothelial cells" did not express Vezf1.

Applicants' arguments regarding using the Vezf1 gene as a marker for vascular endothelial cells do not relate to claims 2 and 4-6, which are limited essentially to a vector comprising a Vezf1 gene. Nowhere does the specification assert such a vector can be used to mark endothelial cells.

Asserting the Vezf1 gene is a marker for the genus of "endothelial cells" on pg 7, lines 11-13, is inadequate for one of skill to know or guess that the Vezf1 gene is actually a marker only for vascular endothelial cells.

Applicants argue they need only show partial success in achieving a useful result. Applicants cite MPEP 2107.01 and state the invention must only be capable of performing some beneficial function. Applicants' arguments are not persuasive. The gene is capable of performing some beneficial function, i.e. marking vascular endothelial cells; however, in this case, the specification did not identify the utility of the gene specifically enough and no artisan would have guessed that the asserted utility was limited to vascular endothelial cells. Further research would have been required to determine the Vezf1 gene was limited as a marker for vascular endothelial cells; therefore, the asserted utility does not rise to the level of a substantial utility.

Applicants cite pg 41, line 8, pg 43, line 11, 43, line 13, though pg 45, line 3, and argue the specification provides adequate guidance for one of skill to determine Vezf1 expression was occurs in vascular endothelial cells. Applicants' argument is not persuasive. While applicants disclose observing different Vezf1 expression in vascular endothelial cells and other tissues, applicants did not teach Vezf1 expression was specific to vascular endothelial cells and did not compare Vezf1 expression vascular endothelial cells with other types of endothelial cells. It is not readily apparent from Fig. 9-12, pg 41, line 8, to pg 43, line 11, that Vezf1 was specific to vascular endothelial cells because other endothelial cells were not tested. Without such guidance, the asserted

utility on pg 7, lines 11-13, is not specific because it is not specific to vascular endothelial cells and does not state expression occurs only in vascular endothelial cells.

Applicants' discussion of Xiong and Aitsebaomo is noted. However, the specific utility described by Xiong and Aitsebaomo, i.e. using the Vezf1 gene as a marker for vascular endothelial cells, is missing from the specification as originally filed. While Xiong and Aitsebaomo confirm the asserted non-specific utility in the specification on pg 7, Xiong and Aitsebaomo confirm that failed to teach the Vezf1 gene could only be used as a marker for vascular endothelial cells. One of skill would not have been able how to properly use the Vezf1 gene as a marker for the broad genus of endothelial cells given the teachings in the specification as originally filed.

Applicants argue post-filing evidence is acceptable to support utility. Applicants' argument is not persuasive. While post-filing evidence is acceptable to support utility, in this case, the post-filing evidence provides a utility that is more specific than the one originally asserted and could not have been guessed from the specification as originally filed. The broad asserted utility in specification as originally filed (using Vezf1 as a marker for endothelial cells) does not correlate with the specific utility described by Xiong and Aitsebaomo (using Vezf1 as a marker for vascular endothelial cells).

Applicants' argue they are not required to prove restriction of Vezf1 to vascular endothelial cells. Applicants argue they need only show there is a reasonable correlation between the activity in question and the asserted utility. Applicants' argument is not persuasive. There is not a reasonable correlation between the activity in question (using Vezf1 as a marker for vascular endothelial cells) and the asserted

utility. One of skill could not have realized from the specification as originally filed that the Vezf1 gene was only usable as a marker for vascular endothelial cells. The examiner agrees that one of skill would have realized from the specification that Vezf1 was a marker for vascular endothelial cells. However, one of skill would not have known the Vezf1 could only be used to mark vascular endothelial cells as taught by Xiong and Aitsebaomo, which does not correlate in scope to the broad asserted utility on pg 7, lines 11-13. The limited scope of use - only for marking vascular endothelial cells - was not originally disclosed and is considered essential to use Vezf1 as a marker gene. In this case, the broad asserted utility is less likely to be true because of the numerous species of endothelial cells within the genus that do not express Vezf1, i.e. lymph vessels, pericardium, peritoneum, or pleura, saliva glands and other serous glands.

Applicants reiterate their arguments regarding the Stuhlmann declaration, which teaches Vezf1 would be useful for identifying endothelial cells and detecting arterial injury (3rd ¶). The declaration was not persuasive in the office action of 12-9-05. Using Vezf1 to identify endothelial cells lacks specific utility because Xiong 1999 taught Vezf1 was specific to vascular endothelial cells and because the specification on pg 7, lines 11-13, only teaches identifying endothelial cells using Vezf1. The specification does not teach Vezf1 is specific to endothelial cells or that Vezf1 is specific to vascular endothelial cells as described by Xiong 1999. The declaration teaches endothelial cells only express Vezf1 when proliferation is required which is not described in the specification. The specification concludes "Vezf1 expression is mainly confined to

vascular endothelial cells and their precursors;" the specification does not conclude that Vezf1 expression is limited to proliferating vascular endothelial cells.

The asserted utilities in the specification have been addressed more specifically in the office action of 5-26-04 as follows:

Pg 7, 3rd full paragraph, states the invention provides for a method of identifying an endothelial cell by identifying expression of Vezf1 RNA or protein in the cell. However, applicants do not provide a reasonable correlation between Vezf1 expression and endothelial cells. The specification and the art at the time of filing do not teach that Vezf1 expression occurs only in endothelial cells; therefore, the asserted utility is not substantial. Pg 41, 1st full ¶, last sentence, states Vezf1 expression correlates to the beginning of blood island formation; it does not state Vezf1 expression in blood islands was limited to endothelial cells. Endocardial cells, which inherently comprise endothelial cells, did not express Vezf1 (¶ bridging pg 41-42, 2nd sentence; AP staining indicates Vezf1 expression as described in the preceding ¶). Strong expression was found in the allantois (pg 42, lines 5-6); however, the specification does not teach expression in the allantois was limited to endothelial cells. The specification concludes, "Vezf1 expression is mainly confined to vascular endothelial cells and their precursors." The term "mainly" in the statement implies more than just endothelial cells express Vezf1 or that non-endothelial cells expressed Vezf1; therefore the asserted utility is not specific. The conclusion that vascular endothelial cells and their precursors express Vezf1 implies that the asserted utility would be generic to vascular endothelial cells and their precursors. Such a utility is not specific to one type of cell because endothelial

cells and endothelial cell precursors have different structures and functions. At the time of filing applicants had merely begun to establish an expression pattern for Vezf1, which in and of itself is insufficient to establish a specific utility for using the Vezf1 gene as a marker for endothelial cells because Vezf1 gene expression is generic to vascular endothelial cells, their precursors and possibly other types of cells that have not been tested, and because Vezf1 expression did not occur in endothelial cells of the endocardium (¶ bridging pg 41-42).

Pg 7, 4th full paragraph, discusses using the Vezf1 gene to diagnose vascular disease. However, the specification and the art at the time of filing do not correlate Vezf1 expression with any vascular disease; therefore, the asserted utility is not specific to any vascular disease. In addition, the specification does not teach whether vascular disease correlates with overexpression or lack of expression of Vezf1; therefore, the asserted utility is not substantial. Finally, the specification does not describe any vascular diseases linked to overexpression of Vezf1 or a disruption in Vezf1; therefore, the asserted utility is not substantial.

Pg 7, 4th full paragraph, discusses using Vezf1 to treat vascular disease. However, the specification and the art at the time of filing do not correlate Vezf1 with any vascular disease; therefore, the asserted utility is not specific to any vascular disease. In addition, the specification does not teach whether vascular disease correlates with an excess or an absence of Vezf1; therefore, the asserted utility is not substantial. Finally, the specification does not describe any vascular diseases linked to an excess or an absence of Vezf1; therefore, the asserted utility is not substantial.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on 571-272-0735.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER